L Number	Hits	Search Text	DB	Time stamp
1	326	porpus WITH alginate	USPAT;	2003/01/23 14:13
			US-EGPUB;	
			EPO; JPO;	
			DERWENT	
7	104		USEAT;	2003/01/23 14:19
		nual-di on RNA or sequence\$1 or nucleic)	T3-F3FUB;	
			EPI; CPI;	
2.5	-	. AND HARLOCACE OF	DEFWENT	2003 01 23 14:31
13	2	w: NFAE "4953656"	WSEAT;	1.000 01 50 141
1			BEI, CEC,	
			DESWENT	
19	2	w: NEAE "4715195"	TSEAT;	2003 01 23 14:21
	•~		TS-EGHUE;	
			ERPI; CPI;	
			DEEWENT	
31	23	US-5042446-3 or US-6743416-\$ or	TSTAT;	.1003 01 .13 14:28
		UC-+381915-\$ or US-6381256-\$ or	US-PGHUE;	
		U2+00104 (4-\$ or U3-58858, 3-\$ or	EPI;	
		US-0-3-475-\$ on US-5496420-\$ on	DEFWEIT	
		US-4+3:155-5 er US-4718801-4 er		
		US-10607.7-\$ or US-6071490-\$ or		
		U2-1853 N2-\$ on U2-554.3:5-\$ on		
		US-AMTHALD-\$ or US-86898 (6-\$).did. or - MS0009046678-\$).and. r (US-5985829-\$		
		1,855,000,004,657,547,414,		
		W(0-981, 17.8-4) = 0.0000000000000000000000000000000000		
		W0-0748532-\$9.dia. on W0-9428874-\$ or		
		W0		
36	21	U5942496-\$ or U3-5762416-\$ or	USFAT;	1:003 01723 15:07
		US-0281/15-4 or US-6281256-4 or	US-PGHUE;	
		US-5016404-3 or US-8980813-\$ or	ELENCY CIPO;	
		US-5639473-4 on US-5496400-\$ on	DEFWELT'	
		03-4783188-8 or 03-4718861-\$ or		
		US-4666 U-\$ Or US-6071495-\$ Or		
		U3-5-8:750-\$ or U3-88479:8-\$ or		
		US-5 771721-4 or US-8889878-44.aid. or		
		WS-10011048672-\$).aid. ir (WS-5885829-\$		
		o: W0-4423346-3 or U3-3716494-3 or		
		With And LLL Braining Monage 1-414-\$ in the control of the control		
		W0-814 1128-3		
		nucleic DMA		
43	2:	: Nucleik in MA 	USFAF;	2003 01 23 15:22
1-	<i>-</i> .	173-4181 13-\$ 12 73-6381288-\$ 12	US-PGIUE;	2000 01 20 10.52
			EFC; CFC;	
		โซซะคิทธิวิจาซิ-จิ้ง ฮิย โซซะคิจจิจจิจิวิย	DEFWENT	
		V3-4-83/161-4 pr V3-471-861-4 pr		
		V3-4486707-\$ 5% V3-6070498-\$ 5%		
		TX=N983 12=\$ 55 TX=8841938=\$ 55		
		78-575.17-\$ ir 73-555.575-\$.aid. or	!	
		US00.0046673-\$0.dad.cr/0US-8685629-\$	1	
		or WC+4405336-3 or US-5716414-\$ or		
1		W0- G10218-\$ or W0-8616414-\$ or		
		W(- 5745537-\$).did. or W(-9428874-\$ or		
		WC-3056(56-\$).did. and :poro\$4 pore\$1 algunate nucleuc DNA)		
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120	JII	iggua pha pha) SAME (poroșe poreși algunăt: nucleic INA)	US-PGIUE;	1.000 01.70 10:20
		augunate maciolo invar	EPC; CFO;	
			DEFWENT	
55	214	(porc\$4 pore\$1	USPAT;	2003/01/23 15:27
	214	algunate rucleic ENA)) and alginate	US-PGPUB;	1
			EPO; JPO;	
			DEFWENT	
61	140	(pglapgapla) SAME (poro\$4 pore\$1	USEAT;	2003.01,23 15:27
		algina (Lucleic ENA)) and alginate and	US-PGPUE;	
1		·	1	1
		gel	EPO; JFC;	

- 135 BONADIO USFAT; UC-PSPU EPU; JP DEFWENT UM DR - 10 BONADIO and jeffrey.in. BONADIO and seffrey.in. BONADIO and SHEA.in. USFAT; USFAT;	2)02/05/01 15:50 6; 1;
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- 10 BONADIO and jeffrey.in. USEAT; US-PGPU EPC; JE USEWENT USCCE 1 BONADIO and SHEA.in. USEAT;	2 002 005 01 15:50 5; 1;
- 10 BONADIG and jeffrey.in. USFAT; US-PGPU EPC; JE USEWENT USGCE 1 BONADIG and SHEA.in. USFAT;	:
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- 1 BONADIC and SHEA.in. USEAT;	
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- 1) BONADII and goldstein.in. "SFAT;	2002/05/01 16:12
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- 2 ("6261,55").PM. "/FAT;	2000 05-11 16:15
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- 14 m:onεy-david-j.in. Π.ΕΑΤ;	2002:05/11 17:16
TU-PGPU	.
Fig. 3F	!
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11.4 - Paint	÷;
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- 14012 pinous NEAR polymer or microsphere or "SHAT;	2002 35 01 17:20
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- 1170 (portus NEAR (polymer or microsphere or UCFAT;	2000-05/01 17:21
gel in hydrogel or matrix or alignate))	
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- 158 (openous NEAR (polymer or microsphere or USEAT;	2002/05.01 17:42
gel or hyprogel in matrix or alignate)) "T-FORUS	P;
and (DMA or FNA ir nucleic or gene)) and API; JP	
(ELGA or lactic\$15) DEFWENT	
1 Diegs	
- 62 (Coporcus NEAR (polymer or microsphere or TGFAT;	2002 05/01 17:46
gel or hydrogel or matrix or alignate))	
and (EMA or EMA ir nucleuc or gene)) and (EMB Dr.	
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- 16 ((portus NEAR (polymer or microsphere or MOFAT;	.:00:::05::01 17:47
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gel or hydrogel or matrix) UN-DOPUI	
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HMOCE.	
- 6793 (porous NEAR (polymer on microsphere or UNEAT;	2002,09/19 15:18
gel or hydrogel or matrix)) and gas\$5 UN-PGPU	
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USC CF.	

-	6521	pordus NEAR (polymer or microsphere or	USPAT;	2002/09/19 15:18
		gel or hydrogel or matrix)) and gas	US-FGPUP;	
			EPO; JPO;	
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_	1424	(porpus NEAR (polymer or microsphere or	TSLAT;	20 (20) 19 15:25
	144	qel or hydrogel or matrix)) and qas) and	US-POPUF;	
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_	15	perpus NEAF (polymer or microsphere or	USFAT;	2002/09/19 15:30
		gel or hydrodel or matrix) NEAR gas	US-MORUE;	
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			USIME	
_	1193	pcrous NEAR (polymer or microsphere or	TSEAT;	2002/09/19 16:42
		gel or hydrogel or matrix) AND gas AND	OS-EGPUE;	
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			USAGE USEAT;	0000009 19 15:37
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1		(DMA in nucleic or sequence)) and	EP1; JP1;	
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_	1	alignate SAME (nucleic or DNA)	TSFAT;	1.003.09.19.15:35
			US-FGFUB;	
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			TSGGF	
_	4.4	alginate AND (nucleic or DNA)	USFAT;	2002 09 19 15:58
			US-FGPUB;	
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	0.5.1	The state of the s	73105	10
-	251	(alginate AND (nucleic or DNA)) and	TSPAT;	3003709 19 15:45
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_	6.1	((alginate AND (nucleic or ENA)) and	USFAT;	2000 09 19 15:53
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-	3.1	(((alginate AND nucleic or DNA)) and	TSPAT;	200.000 19 15:54
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		and gas	EPO; CPO;	
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_	1.	(((alginate AND nucleic or ENA)) and	USEAT;	200 09/19 15:54
	1	alginate.clm.) and inucleic or ENA).clm.)	US-PGFUB;	1.000. 7 0.007 1.0 10 10 4
		and gas.clm.	EP1; CEC;	
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_	693	(alginate AND (nucleic or DNA) and	USEAT;	200: 09/19 15:59
		porous	US-PGFUE;	
			EPO; JPO;	
			DESWENT;	
			USCOP	
-	355	((alginate AND (nucleic or ENA)) and	USFAT;	2001 09/19 15:59
		porous) and gas	US-PGPUB;	
			EPC; JPC;	
			IEPWENT;	
_	96	(((porcus NEAR (polymer or microsphere or	USICE USEAT;	2002/09/19 16:05
	-''	gel or hydrogel or matrix,) and gas) and	US-FGPUP;	UU, U_J, I I I I U I U I
		gas.clm.) and leach\$5	EPO; JPO;	
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DNA or nucleic or sequence) and leach\$5 ED; (Po; DEFWEIT; USC)2 DEFWEIT; USC)3 DEFWEIT; USC)4 DEFWEIT; USC)4 DEFWEIT; USC)5 DEFWEIT; USC)5 DEFWEIT; USC)6 DEFW	_	1/1			TOOT'' AND TO: 0
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- 13 'pporous NEAF (polymer or microsphere or gel or hydrogel or matrix: AND gas AND (US-DELUE; (DNA or nucleic or sequence)) and 435/325 (EPG; CPG; DES-MENT; USCOP) (UNA or nucleic or sequence)) and 435/325 (EPG; CPG; DES-MENT; USCOP) (UNA or nucleic or sequence)) and 435/325.cols. - 21 microsphere3 SAME gas SAME (DNA or USLAT; USCOP) (DES-MENT) (USCOP) (USAGE)			(D.A of nucleic or sequence) and leach\$5		
- 13 (percus NEAF (polymer or microsphere or get or hydrogel or matrix) AND gas AND (SFAT; US-PGIUE; (DUA or nucleic or sequence)) and 435/325 (DERWEIT; US-PGIUE; (DERWEIT) (DE					
del or hydrogel or matrix) AND gas AND S3-PGSUE; EPO; UPO; DEPMENT; DEPM					
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- 12 (percus NEAF (polymer or microsphere or get or hydrogel or matrix) AND gas AND (INA or nucleic or sequence)) and (INA or nucleic or sequence)) and (25,725,5cls.) - 21 microsphere33 SAME gas SAME (BNA or nucleic) - 4 "191" and leach\$5 (DSCOP) - 4 "191" and leach\$5 (DSCOP) - 46 433/725,5cls. and leach\$5 (DSCOP) - 47 433/725,5cls. and leach\$5 (DSCOP) - 48 433/725,5cls. and leach\$5 (DSCOP) - 49 433/725,5cls. and leach\$5 (DSCOP) - 40 50 70 70 70 70 70 70 70 70 70 70 70 70 70				· ·	
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nucleic)	_	21	microsphere\$3 SAME gas SAME (DNA or	USEAT;	1:00::/09/19 16:39
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TSOCF TSEAT; US-PSIUE; EP1; CP0; DEFWENT; US-OF USEAT; US-PGIUE; EP6; CP0; DEFWENT; USCCF USEAT; US-PGIUE; EF6; CP0; DEFWENT; USCCF USCCF USEAT; US-PGIUE; EF0; CP0; DEFWENT; USCCF USCCCF				EPO; CPO;	1
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TS-PGFUB; EPT; CPO; DEFWENT; USCOS USEAT; US-PGFUB; EFC; CPO; DEFWENT; USCOS USCOS USCOS 1418 435/\$3.ccls. and leach\$5				USCOF.	
#P1; \PD; DEFWENT; USFORF 46 435/325.ccls. and leach\$5 - 46 435/325.ccls. and leach\$5 - 1418 435/\$3.ccls. and leach\$5 - 1418 435/\$3.ccls. and leach\$5 - 32 (perous NEAR (pelymer or microsphere or USFAT; USFORF DEFWENT;	-	41	"151" and leach\$5		2002/09/19 16:40
DEPWENT; USOCF USEAT; US-PGFUB; EFG; CFG; BEFWENT; USCCF USEAT; US-PGFUB; EFG; CFG; BEFWENT; USCCF USEAT; US-PGFUB; EFG; CFG; DEFWENT; USCCF USEAT; US-PGFUB; EFG; CFG; DEFWENT; USCCF USEAT; USCCF USCAT; USCAT; USCCF USCAT; USCCF USCAT; USCCF USCAT; USCAT; USCCF USCAT; U				US-PGFUE;	
- 46 43%/325.cols. and leach\$5 USSAT; US-PGFUB; EFC; UFO; DEFWENT; USCOF - 1418 43%/\$3.cols. and leach\$5 USSAT; USCOF - 32 (percus NEAF (polymer or microsphere or gel or hydrogel or matrix) AND gas AND (US-PGFUE; (DNA or nucleic or sequence)) and (EFC; UFO; USFWENT; USCOF) (455/\$3.cols. and leach\$5) USCOF USCO				EPO; CPO;	
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US-PGFUB; EFC; CFO; DEFWENT; USCOF USFAT; US-PGFUB; EFC; CFO; DEFWENT; USCOF USFAT; US-PGFUB; EFC; CFC; (DNA or nucleic or sequence); and EFC; CFO; (435/\$3.ccls. and leach\$5) DEFWENT;				USAADE	
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EPC; CPC; DEFWENT; USCCE 32 (porous NEAF (polymer or microsphere or USEAT; gel or hydrogel or matrix) AND gas AND US-PGPUE; (DNA or nucleic or sequence)) and EFO; CPO; (455/\$3.ccls. and leach\$5) DEFWENT;	}			US-PGIUE;	
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L1 1419 S ALGINATE (L) POR?

L2 435 S L1 AND GEL

76 S L1 AND (DNA OR RNA OR NUCLEIC OR PLASMID OR VECTOR OR SEQUENC

L4 40 DUP REM L3 (36 DUPLICATES REMOVED)

L5 40 FOCUS L4 1-

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L5 ANSWER 1 OF 40 CAPLUS COPYRIGHT 2003 ACS

AN 1999:736893 CAPLUS

DN 131:332976

L3

TI Sustained **dna** delivery from structural porous matrices for gene therapy applications with special emphasis is on bone formation and regeneration

SO PCT Int. Appl., 144 pp.

CODEN: PIXXD2

IN Shea, Lonnie D.; Bonadido, Jeffrey; Mooney, David J.

Disclosed are particular 3-dimensional structural matrixes contg. ${\tt DNA}$ and their use in the prolonged release of ${\tt DNA}$ in various biol. environments. The structural matrix is a porous polymer [PLGA]-based contg. pores formed by gas foaming involving inert gases (CO2) and leaching out of a water-sol. particulate (salt, NACL, sugar, glucose, sucrose, mannitol) when exposed to body fluids. The admixt. is compression molded into a selected size and shape prior to executing the gas foaming process. The structural matrix may also be an alginate or modified alginate matrix. This structural matrix is a biocompatible or biodegradable matrix. It may also be a lactic acid polymer, glycolic acid polymer or lactic acid/glycolic acid copolymer matrix. At least part of this matrix may be comprised of lactic acid/qlycolic acid (PLGA) copolymer matrix. The structural matrix may be modified where one side section is bonded to one cell interaction mol. such as cell adhesion mols., cell attachment peptides, proteoglycan attachment peptide sequences, proteoglycans, cell adhesion polysaccharides, growth factors, cell adhesion enzymes, RGD peptide, fibronectin, vitronectin, Laminin A, Laminin B1, Laminin B2, collagen 1 and thrombospondin. The DNA-matrix materials are created such that they maintain a defined space, allowing cellular migration, transfection and proliferation to occur in a controlled manner. Such DNA-contg. structural matrixes are thus particularly useful in in vivo cell transfection and gene expression in the context of gene therapy. This may encode a protein for stimulating bone progenitors or wound healing in fibroblast or in tissue or organ regeneration or transplantation or an antigen for immunity or cytotoxic or apoptosis-inducing protein or a transcription factor or elongation factor or cell cycle control protein or kinase or phosphatase or DNA repair protein or oncogene or tumor suppressor or angiogenic protein or anti-angiogenic protein or immune response stimulating protein or cell surface receptor or accessory signaling mol. or transport protein or anti-bacterial or anti-viral protein or hormone or neurotransmitter or growth factor or growth factor receptor or interferon or interleukin or chemokine or cytokine or colony stimulating factor or chemotactic factor protein of growth hormone cr parathyroid hormone or PTH1-34 polypeptide or bone morphogenic protein or BMP-2A or BMP-2B or BMP-3 or BMP-4 or BMP-5 or BMP-6 or BMP-7 or BMP-8 or TGF-.alpha. or TGF-.beta.1 or TGF-.beta.2 or latent TGF.beta. binding protein or activin/inhibin protein or FGF or GMCSF or EGF or PDGF or insulin-like growth factor or leukemia inhibitory factor. This method allows for the use in gene transfer to cells within a tissue site and in manuf. of a medicament for gene therapy. Implantable medical devices comprising this gene-matrix are described. The release of nucleic acids from the matrix is controlled by diffusion. This method also applies to cancer therapy or treating viral infection. PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 9958656 A2 19991118 WO 1999-US10330 19990512 WO 9958656 A3 20000106

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Elastins
Enzymes, biological studies
Fibrins
Fibroblast
Fibronectins
Glass, biological studies
Globins
Hematopoietic precursor cell
Hormones, animal, biological studies
Immunoglobulins
Interferons
Interleukin 2 receptors
Interleukins
Laminins
Myoblast
Neuroglia
Osteoblast
Peptides, biological studies
Platelet-derived growth factors
Polyamide fibers, biological studies
Polyester fibers, biological studies
Polyesters, biological studies
Polysulfones, biological studies
Proteoglycans, biological studies
Receptors
Silk
Tenascins
Transforming growth factors
Vaccines
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
   (hybrid matrix implants and explants)
Drug delivery systems
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
   (implants; hybrid matrix implants and explants)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
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Drug delivery systems
PL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
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Nerve
PL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
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  (smooth, cells; hybrid matrix implants and explants)
Pancreatic islet of Langerhans
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
   (.beta.-cell; hybrid matrix implants and explants)
9001-27-8, Factor VIII 9001-28-9, Factor IX 9002-64-6, Parathyroid
         9003-05-8, Polyacrylamide 9003-53-6, Polystyrene
hormone
Insulin, biological studies 9004-34-6, Cellulose, biological studies
9004-54-0, Dextran, biological studies 9004-61-9, Hyaluronic acid
9005-32-7, Alginic acid 9005-35-0, Calcium alginate 9007-12-9,
Calcitonin 9012-36-6, Agarose 9041-92-3 9050-30-0, Heparan sulfate 11096-26-7, Erythropoietin 12629-01-5, Human growth hormone 24967-94-0, Dermatan sulfate 37228-64-1, Glucocerebrosidase
62229-50-9, Epidermal growth factor 62683-29-8, Colony stimulating
factor 67763-96-6, Insulin-like growth factor 1 83869-56-1,
Granulocyte-macrophage colony stimulating factor 106096-92-8, Acidic
fibroblast growth factor 106096-93-9, Basic fibroblast growth factor
139639-23-9, Tissue plasminogen activator 143011-72-7, Granulocyte
colony stimulating factor 169494-85-3, Leptin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
   (hybrid matrix implants and explants)
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ΙT

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W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BJ, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

AU 9938986 A1 19991129 AU 1999-38986 19990512
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L9 ANSWER 21 OF 24 CAPLUS COPYRIGHT 2003 ACS
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AN 1997:377878 CAPLUS

DN 126:347315

TI Hybrid matrix implants and explants

SO PCT Int. Appl., 50 pp. CODEN: PIXXD2

IN Mineau-Hanschke, Rochelle

An implantable device having a body of matrix material made up of insol. collagen fibrils, and disposed therewithin: (a) a plurality of vertebrate cells; and (b) a plurality of microspheres each of which consists primarily of one or more of the following materials: collagen, polystyrene, dextran, polyacrylamide, cellulose, calcium alginate, latex, polysulfone, or glass. A clonal cell strain of human fibroblasts stable transfected with the plasmid pXGH302 secreting recombinant human growth hormone was prepd. and combined with porous collagen microspheres in a hybrid matrix.

									IND DATE APPLICATION NO. DATE									
ΡI	WO	9715	195		A	1	1997	0501		WO	19	96-U:	S171:	14	1996	1025	<	
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TΤ
     Hybrid matrix implants and explarts
ΙN
     Mineau-Hanschke, Rochelle
     Transkaryotic Therapies, Inc., USA
PΑ
     PCT Int. Appl., 50 pp.
SO
     CODEN: PIXXD2
     Patent
DT
LA
     English
     ICM A01N063-00
TC
     ICS A01N065-00; A61K048-00; A61F013-00; C12N005-16; C12N015-16;
          C12N015-85; B01D063-00
CC
     63-6 (Pharmaceuticals)
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                                           APPLICATION NO. DATE
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     WO 9715195 A1 19970501 WO 1996-US17114 19961025 <--
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        917428 A1 19990526 EP 1996-936960 19961025
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NO 9801859 A
AU 736255 B2
PRAI US 1995-548002 A
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                            19980624
                                           NO 1998-1859
                            20010726
                                           AU 1999-48841
                                                             19990921
                            19951035
     WO 1996-US17114 W 19961025
     An implantable device having a body of matrix material made up of insol.
AB
     collagen fibrils, and disposed therewithin: (a) a plurality of vertebrate
     cells; and (b) a plurality of microspheres each of which consists
     primarily of one or more of the following materials: collagen,
     polystyrene, dextran, polyacrylamide, cellulose, calcium alginate
     , latex, polysulfone, or glass. A clonal cell strain of human fibroblasts
     stable transfected with the plasmid pXGH302 secreting
     recombinant human growth hormone was prepd. and combined with
     porous collagen microspheres in a hybrid matrix.
ST
     hybrid matrix implant explant
ΙT
     Lipoprotein receptors
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
       (LDL; hybrid matrix implants and explants)
     Adipose tissue
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (adipocyte; hybrid matrix implants and explants)
ΤТ
     Kidney
    Muscle
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
       (cells; hybrid matrix implants and explants)
     Liver
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (hepatocyte; hybrid matrix implants and explants)
ΙT
     Collagens, biological studies
     RL: FEP (Physical, engineering or chemical process); THU (Therapeutic
    use); BIOL (Biological study); PROC (Process); USES (Uses)
        (hybrid matrix implants and explants)
    Angicgenic factors
    Antibodies
    Antigens
    Blood-coagulation factors
    Chondrocyte
    Cotton
    Cytokines
      DNA
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             87 S L1 AND (DNA OR RNA OR NUCLEIC OR PLASMID OR VECTOR OR SEQUENC
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     ANSWER 24 OF 24 CAPLUS COPYRIGHT 2003 ACS
    1999:159891 CAPLUS
DN
    130:342815
ΤI
     Synthetic extracellular matrixes to guide tissue formation
ΑU
     Peters, Martin C.; Mooney, David J.
     Department of Biomedical Engineering, University of Michigan, Ann Arbor,
     MI, 48109-1078, USA
SO
     International Congress Series (1998), 1170 (Tissue Engineering
     for Therapeutic Use 2), 55-65
     CODEN: EMMDA4; ISSN: 0531-5131
PB
    Elsevier Science B.V.
DT
     Journal; General Review
LA
     English
CC
     63-0 (Pharmaceuticals)
     Section cross-reference(s): 16
     A review with 44 refs. Tissues engineered from cultured cells may
     potentially be utilized to treat a variety of diseases, but techniques to
     promote the development of proper tissue structure and function must first
     be developed. The native extracellular matrix (ECM) of tissues aids this
     process during development by providing mech. support to the forming
     tissue, localizing cells to specific locations, and regulating
     gene expression. Many investigators are attempting to create
     synthetic analogs to the ECM that will serve these functions, and promote
     new tissue formation from cultured cells. We propose to utilize
     combinations of macrostructures to provide tissue-level control of
     structure with hydrogels to provide cell-level guidance over cell
     function. Highly porous fiber-based and sponge-based
     macrostructures have been formed from biodegradable synthetic polymers,
     e.g., polyglycolic acid, using a variety of polymer processing methods.
     Proper design leads to synthetic ECM which provide mech. support for the
     developing tissue, and quidance for the development of gross tissue
     structure. In addn., sol. chem. signals, e.g., protein growth factors,
     can be delivered to cells utilizing these matrixes. We are also currently
     developing hydrogels in which cells within the macrostructures can be
     immobilized. These matrixes are in intimate contact with the cells and
     provide guidance, at the cell level, over tissue structure and function.
     Alginates (polysaccharides derived from seaweed) have been
     covalently modified to allow specific cellular recognition and adhesion.
     These synthetic ECM have shown promise to engineer a variety of tissues,
     including smooth muscle and dental pulp.
ST
     review tissue formation extracellular matrix
     Animal tissue
     Animal tissue culture
        (synthetic extracellular matrixes to guide tissue formation)
IΤ
        (tissue; synthetic extracellular matrixes to guide tissue formation)
     9005-32-7, Alginic acid 26009-03-0, Polyglycolic acid 26124-68-5,
     Polyglycolic acid
     RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
     use); BIOL (Biological study); PROC (Process); USES (Uses)
        (synthetic extracellular matrixes to guide tissue formation)
RE.CNT 44
             THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
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             40 FOCUS L4 1-
I.E.
             87 S L1 AND (DNA OF RNA OF NUCLEIC OR PLASMID OR VECTOR OR SEQUENC
L7
             45 DUP REM L6 (42 DUPLICATES REMOVED)
             24 S L7 AND PY<=1998
1,4
             24 SORT L8 PY
L10
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     ANSWER 21 OF 24 CAPLUS COPYRIGHT 2003 ACS
ΑN
     1997:377878 CAPLUS
DN
     126:347315
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(FILE 'HOME' ENTERED AT 13:39:01 ON 23 JAN 2003) FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED AT 13:39:09 ON 23 JAN 2003 26 S POROUS ALGINATE 15 DUP REM L1 (11 DUPLICATES REMOVED) L2 L3 15 SORT L2 PY 449 S POROUS (L) ALGINATE L415 S L4 AND (DNA OR NUCLEIC OR GENE) L5 10 DUP REM L5 (5 DUPLICATES REMOVED) 1.7 10 SORT L6 PY L₈ 319 S L4 AND PY<=1998 262 DUP REM L8 (57 DUPLICATES REMOVED) L9 L10 50 S L9 AND PORE? L1165 S L9 AND (PORE? OR GAS) L12 65 FOCUS L11 1-4 S L9 AND (DNA OR NUCLEIC OF GENE OR DEOXY? OR RNA OR RIBO? OR L13 => d 113 2 all L13 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS 1997:377878 CAPLUS 126:347315 DN Hybrid matrix implants and explants ΙN Mineau-Hanschke, Rochelle PΑ Transkaryotic Therapies, Inc., USA SO PCT Int. Appl., 50 pp. CODEN: PIXXD2 DT Patent LA English ICM A01N063-00 ΙC ICS A01N065-00; A61K048-00; A61F013-00; C12N005-16; C12N015-16; C12N015-85; B01D063-00 63-6 (Pharmaceuticals) FAN.CNT 4 PATENT NO. KIND DATE APPLICATION NO. DATE WO 9715195 A1 19970501 WO 1996-US17114 19961025 <--PΙ W: AL, AM, AT, AU, AI, BB, BG, BR, BY, CA, CH, CN, CU, CI, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA A 19991012 US 1995-548002 19951025 A1 19970515 AU 1996-74744 19961025 US 5965125 AU 9674744 19961025 <--B2 19990617 AU 706563 CN 1996-199324 19961025 EP 1996-936960 19961025 CN 1205613 A 19990120 EP 917428 Al 19990526 R: AT, BE, CH, DE, DK, ES, FF, GE, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO BR 9611248 A 19991228
JP 2000501299 T2 20000208
NO 9801859 A 19980624 BR 1996-11248 19961025 JP 1997-516803 19961025 NO 1998-1859 19980424 <--AU 736255 B2 PRAI US 1995-548002 A 20010726 AU 1999-48841 19990921 19951025 WO 1996-US17114 W 19961025 An implantable device having a body of matrix material made up of insol. collagen fibrils, and disposed therewithin: (a) a plurality of vertebrate cells; and (b) a plurality of microspheres each of which consists primarily of one or more of the following materials: collagen,

polystyrene, dextran, polyacrylamide, cellulose, calcium alginate , latex, polysulfone, or glass. A clonal cell strain of human fibroblasts stable transfected with the plasmid pXGH302 secreting recombinant human growth hormone was prepd. and combined with porous collagen microspheres in a hybrid matrix.

ST hybrid matrix implant explant

Lipoprotein receptors

RL: THU (Therapeutic use); BICL (Biological study); USES (Uses)

(LDL; hybrid matrix implants and explants) Adipose tissue RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (adipocyte; hybrid matrix implants and explants) ΤТ Kidney Muscle RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (cells; hybrid matrix implants and explants) ТТ Liver RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (hepatocyte; hybrid matrix implants and explants) Collagens, biological studies RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (hybrid matrix implants and explants) ΙT Angiogenic factors Antibodies Antigens Blood-coagulation factors Chondrocyte Cotton Cytokines DNA Elastins Enzymes, biological studies Fibrins Fibroblast Fibronectins Glass, biological studies Globins Hematopoietic precursor cell Hormones, animal, biological studies Immunoglobulins Interferons Interleukin 2 receptors Interleukins Laminins Myoblast Neuroglia Osteoblast Peptides, biological studies Platelet-derived growth factors Polyamide fibers, biological studies Polyester fibers, biological studies Polyesters, biological studies Polysulfones, biological studies Proteoglycans, biological studies Receptors Silk Tenascins Transforming growth factors Vaccines RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (hybrid matrix implants and explants) Drug delivery systems RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (implants; hybrid matrix implants and explants) ΤТ RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (keratinocyte; hybrid matrix implants and explants) Drug delivery systems RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (microspheres; hybrid matrix implants and explants) IΤ Nerve RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (neuron, cells; hybrid matrix implants and explants) RL: TH'J (Therapeutic use); BIOL (Biological study); USES (Uses) (smooth, cells; hybrid matrix implants and explants) Pancreatic islet of Langerhans

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- L12 ANSWER 1 OF 65 CAPLUS COPYRIGHT 2003 ACS
- AN 1988:57576 CAPLUS
- DN 108:57576
- TI Porous alginate moldings
- SO Jpn. Kokai Tokkyo Koho, 4 pp. CODEN: JKXXAF
- IN Hirasa, Okihiko
- AB Porous moldings useful in culturing of enzymes, microbes, etc. are prepd. by heating aq. alginates with aq. poly(vinyl Me ether) (I) to the phase transition temp. (T) of I adding aq. metal salts forming insol. alginates, and extg. I with water at temps. below T. A mixt. of 1 part 5% Na alginate and 1 part 30% I was coated (0.5 mm) on glass, dipped for 10 min in 2% CuSO4 at 40.degree., removed from the glass, and extd. with water to give a Cu alginate film with pore diam. 10-50 .mu. and water permeability 70 times that of a film prepd. without I.

PATENT NO. KIND DATE APPLICATION NO. DATE

PI JP 62250040 A2 19871030 JP 1986-93833 19860423 <-JP 05053926 B4 19930811

- L12 ANSWER 2 OF 65 CAPLUS COPYRIGHT 2003 ACS
- AN 1995:869435 CAPLUS
- DN 123:260244
- TI Low-density crosslinked porous hydrogel polymer materials having good compression strength and articles formed therefrom
- SO PCT Int. Appl., 39 pp. CODEN: PIXXD2
- IN Unger, Peter D.; Fohrbach, Ronald P.
- The title materials are prepd. by dissolving a hydrogel polymer selected from alginates, gums, starch, dextrins, agar, gelatins, casein, collagen, poly(vinyl alc.), polyethylenimine, acrylate polymers, starch-acrylate polymers, or mixts. or copolymers thereof in a gelling solvent, forming a gel from the soln. into a form, replacing the gelling solvent with a crosslinking solvent using a conc. gradient solvent-exchange process, and treating the gel with a crosslinking agent to form porous bodies with a open-celled three-dimensional lattice structure, d. <1.0, surface area .gtoreq.30 m2/g, compressibility .ltoreq.10% yield at 10 psi, and av. pore diam. <100 .ANG.. Thus, 5% aq. Na alginate soln. was gelled in 0.2 M CaCl2 soln., formed into cubes, treated with aq. 25% acetone, subsequently treated with aq. 50% acetone, then treated with aq. 50% acetone, finally treated with acetone, treated with a mixt. of 2,4-tolylene diisocyanate and triethylamine, heated 16 h at 100-110.degree.to give a crosslinked hydrogel material with apparent bulk d. 0.164, surface area 380 m2/q, pore vol. 2.97 cm3/g, and av. pore diam. 365 .ANG..

PATENT NO. KIND DATE APPLICATION NO. DATE

PI WO 9512632 A2 19950511 WO 1994-US12645 19941102 <-WO 9512632 A3 19950526
W: JP
US 5502082 A 19960326 US 1993-148110 19931104 <-JP 08505431 T2 19960611 JP 1994-513411 19941102 <--

L12 ANSWER 4 OF 65 CAPLUS COPYRIGHT 2003 ACS

AN 1978:173017 CAPLUS

DN 88:173017

TI Porous material

SO Ger. Offen., 26 pp.

CODEN: GWXXBX

IN Miles, Brynley John

Discrete porous particles for mol. sieve applications are made by mixing a finely distributed, practically insol., absorbent inorg. material in an aq. soln. of a sol. alginate(e.g., Na alginate) to form the slurry into droplets, contacting the droplets with a reagent (e.g., aq. NaCl soln.) to ppt. the sol. alginate as insol. alginate thus producing intermediate particles contg. the inorg. material combined with the pptd. alginate. The alginate is at least partially removed by heating to yield discrete porous particles. The alginate may be pptd. with an acid. A 2nd pore-forming substance may be added to increase or modify the porosity. Thus, TiO2 is slurried in a 1% aq. Na alginate soln. in a ball mill for 5 h, the slurry added in droplets to a 0.1 M NaCl soln. to form discrete particles contg. TiO2 particles bonded by the Ca alginate pptd. The particles are transferred to MeOH, dehydrated, heated to 100.degree. for 1-2 h, and sintered at 900.degree.. Discrete porous TiO2 particles with a diam. of 500.mu. are obtained.

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
ΡI	DE 2727143	A1	19771229	DE 1977-2727143	19770616 <
	DE 2727143	C2	19890323		
	GB 1586364	A	19810318	GB 1976-25209	19760617 <
	SE 7706990	A	19771218	SE 1977-6990	19770616 <
	SE 435717	В	19841015		
	SE 435717	С	19850124		
	NL 7706730	A	19771220	NL 1977-6730	19770617 <
	JP 52154814	A2	19771222	JP 1977-71947	19770617 <
	JP 63023158	B4	19880514		
	SE 8207520	Α	19821230	SE 1982-7520	19821230 <
	SE 451715	В	19871026		
	SE 451715	С	19880204		

(FILE 'HOME' ENTERED AT 13:39:01 ON 23 JAN 2003)

FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED AT 13:39:09 ON 23 JAN 2003

L1 26 S POROUS ALGINATE
L2 15 DUP REM L1 (11 DUPLICATES REMOVED)
L3 15 SORT L2 PY
L4 449 S POROUS (L) ALGINATE
L5 15 S L4 AND (DNA OR NUCLEIC OR GENE)

=> d an ti so au ab pi 17 4 2 3 6 8

10 SORT L€ PY

L7 ANSWER 4 OF 10 CAPLUS COPYRIGHT 2003 ACS

AN 1999:736893 CAPLUS

DN 131:332976

L6 L7

TI Sustained **dna** delivery from structural porous matrices for **gene** therapy applications with special emphasis is on bone formation and regeneration

10 DUP REM L5 (5 DUPLICATES REMOVED)

SO PCT Int. Appl., 144 pp. CODEN: PIXXD2

IN Shea, Lonnie D.; Bonadido, Jeffrey; Mooney, David J.

Disclosed are particular 3-dimensional structural matrixes contg. DNA and their use in the prolonged release of DNA in various biol. environments. The structural matrix is a **porous** polymer [PLGA]-based contg. pores formed by gas foaming involving inert gases (CO2) and leaching out of a water-sol. particulate (salt, NACL, sugar, glucose, sucrose, mannitol) when exposed to body fluids. The admixt. 1s compression molded into a selected size and shape prior to executing the gas foaming process. The structural matrix may also be an alginate or modified alginate matrix. This structural matrix is a biccompatible or biodegradable matrix. It may also be a lactic acid polymer, glycolic acid polymer or lactic acid/glycolic acid copolymer matrix. At least part of this matrix may be comprised of lactic acid/glycolic acid (PLGA) copolymer matrix. The structural matrix may be modified where one side section is bonded to one cell interaction mol. such as cell adhesion mols., cell attachment peptides, proteoglycan attachment peptide sequences, proteoglycans, cell adhesion polysaccharides, growth factors, cell adhesion enzymes, RGD peptide, fibronectin, vitronectin, Laminin A, Laminin B1, Laminin B2, collagen 1 and thrombospondin. The ${\tt DNA\text{-}matrix}$ materials are created such that they maintain a defined space, allowing cellular migration, transfection and proliferation to occur in a controlled manner. DNA-contg. structural matrixes are thus particularly useful in in vivo cell transfection and gene expression in the context of gene therapy. This may encode a protein for stimulating bone progenitors or wound healing in fibroblast or in tissue or organ regeneration or transplantation or an antigen for immunity or cytotoxic or apoptosis-inducing protein or a transcription factor or elongation factor or cell cycle control protein or kinase or phosphatase or DNA repair protein or oncogene or tumor suppressor or angiogenic protein or anti-angiogenic protein or immune response stimulating protein or cell surface receptor or accessory signaling mol. or transport protein or anti-bacterial or anti-viral protein or hormone or neurotransmitter or growth factor or growth factor receptor or interferon or interleukin or chemokine or cytckine or colony stimulating factor or chemotactic factor protein of growth hormone or parathyroid hormone or PTH1-34 polypeptide or bone morphogenic protein or BMP-2A or BMP-2B or BMP-3 or BMP-4 or BMP-5 or BMP-6 or BMP-7 or BMP-8 or TGF-.alpha. or TGF-.beta.1 or TGF-.beta.2 or latent TGF.beta. binding protein or activin/inhibin protein or FGF or GMCSF or EGF or PDGF or insulin-like growth factor or leukemia inhibitory factor. This method allows for the use in gene transfer to cells within a tissue site and in manuf. of a medicament for gene therapy. Implantable medical devices comprising this gene -matrix are described. The release of nucleic acids from the matrix is controlled by diffusion. This method also applies to cancer therapy or treating viral infection. PATENT NO. KIND DATE APPLICATION NO. DATE

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      WO 9958656
      A2 19991118

      WO 9958656
      A3 20000106

                                             WO 1999-US10330 19990512
PΤ
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             KE, KG, KP, KR, K2, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
         MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UL, VN, YU, ZW, AM, AL, BY, KG, KZ, MD, RU, TJ, RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
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             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                       A1 19991129
                                            AU 1999-38986
                                                              19990512
     AU 9938986
     ANSWER 2 OF 10 CAPLUS COPYRIGHT 2003 ACS
     1997:377878 CAPLUS
     126:347315
     Hybrid matrix implants and explants
TT
     PCT Int. Appl., 50 pp.
     CODEN: PIXXD2
TN
     Mineau-Hanschke, Rochelle
     An implantable device having a body of matrix material made up of insol.
     collagen fibrils, and disposed therewithin: (a) a plurality of vertebrate
     cells; and (b) a plurality of microspheres each of which consists
     primarily of one or more of the following materials: collagen,
     polystyrene, dextran, polyacrylamide, cellulose, calcium alginate
     , latex, polysulfone, or glass. A clonal cell strain of human fibroblasts
     stable transfected with the plasmid pXGH302 secreting recombinant human
     growth hormone was prepd. and combined with porous collagen
     microspheres in a hybrid matrix.
                                            APPLICATION NO. DATE
     PATENT NO. KIND DATE
     WO 9715195 A1 19970501 WO 1996·US17114 19961025
PΙ
         W: AL, AM, AT, AU, AE, BB, BG, BR, BY, CA, CH, CN, CU, CE, DE, DK,
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         SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

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                  A 19991012
                                          US 1995-548002 19951025
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                                             AU 1996-74744
                       B2 19990617
     AU 706563
     CN 1205613
                       Α
                             19990120
                                            CN 1996-199324
                                                               19961025
                      A1
                           19990526
                                            EP 1996-936960 19961025
     EP 917428
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             IE, SI, LT, LV, FI, RO
                             19991228
                                             BR 1996-11248
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     BR 9611248
                     A
                                             JP 1997-516803
     JP 2000501299
                        T2
                             20000208
                                                               19961025
                      A
     NO 9801859
                             19980624
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                                                               19980424
     AU 736255
                        B2 20010726
                                             AU 1999-48841
                                                               19990921
     ANSWER 3 OF 10 CAPLUS COPYRIGHT 2003 ACS
     1999:159891 CAPLUS
     130:342815
ΤI
     Synthetic extracellular matrixes to guide tissue formation
     International Congress Series (1998), 1170 (Tissue Engineering for
     Therapeutic Use 2), 55-65
     CODEN: EXMDA4; ISSN: 0531-5131
     Peters, Martin C.; Mooney, David J.
     A review with 44 refs. Tissues engineered from cultured cells may
     potentially be utilized to treat a variety of diseases, but techniques to
     promote the development of proper tissue structure and function must first
     be developed. The native extracellular matrix (ECM) of tissues aids this
     process during development by providing mech. support to the forming
     tissue, localizing cells to specific locations, and regulating
     gene expression. Many investigators are attempting to create
     synthetic analogs to the ECM that will serve these functions, and promote
     new tissue formation from cultured cells. We propose to utilize
     combinations of macrostructures to provide tissue-level control of
     structure with hydrogels to provide cell-level guidance over cell
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function. Highly porous fiber-based and sponge-based macrostructures have been formed from biodegradable synthetic polymers, e.g., polyglycolic acid, using a variety of polymer processing methods. Proper design leads to synthetic ECM which provide mech. support for the developing tissue, and guidance for the development of gross tissue structure. In addn., sol. chem. signals, e.g., protein growth factors, can be delivered to cells utilizing these matrixes. We are also currently developing hydrogels in which cells within the macrostructures can be immobilized. These matrixes are in intimate contact with the cells and provide guidance, at the cell level, over tissue structure and function. Alginates (polysaccharides derived from seaweed) have been covalently modified to allow specific cellular recognition and adhesion. These synthetic ECM have shown promise to engineer a variety of tissues, including smooth muscle and dental pulp.

- L7 ANSWER 6 OF 10 CAPLUS COPYRIGHT 2003 ACS
- AN 2002:118123 CAPLUS
- DN 136:139515
- TI Automatic water toxicant measuring instrument using immobilized photogenic microorganism
- SO Repub. Korean Kongkae Taeho Kongbo, No pp. given CODEN: KRXXA7
- IN Lee, Jeong Geon
- PURPOSE: An automatic water toxicant measuring instrument is provided which measures the light emission of photogenic microorganisms induced by toxicants, in which pretreatment of photogenic microorganisms is not involved so, the app. measures water toxicant easily and economically. CONSTITUTION: An instrument for measuring water toxicant using photogenic microorganisms comprises the following parts: (1) a stage driving part consisting of plural vials which contains test samples and immobilized microorganisms, a movable X-Y stage, a sub-driver connected to the stage, and a controller connected to the sub-driver for controlling the position of the stage; (2) a sample supplying part consisting of an sample inlet, a test sample storage plant, of which one side is connected to an automatic sample collector and other side is connected to an outlet of water, and a sample inlet controller connected to the sample inlet; (3) a luminescence intensity measuring part; and an arithmetic and control part. Immobilized microorganisms are as follows; Photogenic microorganisms such as Photobacterium phosphoreum, Vibrio fischeri, or recombinant microorganisms with lux gene are immobilized on porous matrix such as sodium alginate, strontium alginate,

.kappa.-carrageenan, polyacrylamide, cellulose or agarose. Sample water is sequentially added to aligned vials contg. immobilized photogenic microorganism and the difference of luminescence intensity is measured by luminescence dosimeter before and after the sample injection.

PATENT NO. KIND DATE APPLICATION NO. DATE

- PI KR 2000031934 A 20000605 KR 1998-48198 19981111
- L7 ANSWER 8 OF 10 MEDLINE

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- AN 2001479229 MEDLINE
- TI Three-dimensional cartilage formation by bone marrow-derived cells seeded in polylactide/alginate amalgam.
- SO JOURNAL OF BIOMEDICAL MATERIALS RESEARCH, (2001 Dec 5) 57 (3) 394-403. Journal code: 0112726. ISSN: 0021-9304.
- AU Caterson E J; Nesti L J; Li W J; Danielson K G; Albert T J; Vaccaro A R; Tuan R S
- AB Bone marrow-derived cells are considered as candidate cells for cartilage tissue engineering by virtue of their ability to undergo chondrogenesis in vitro when cultured in high density or when embedded within a three-dimensional matrix in the presence of growth factors. This study evaluated the potential of human bone marrow-derived cells for cartilage tissue engineering by examining their chondrogenic properties within a three-dimensional amalgam scaffold consisting of the biodegradable polymer, poly-L-lactic acid (PLA) alone, and with the polysaccharide gel, alginate. Cells were suspended either in alginate or medium and loaded into porous PLA blocks. Alginate was used to improve cell loading and retention within the construct, whereas the PLA polymeric scaffold provided appropriate mechanical support and stability to the composite culture. Cells seeded in the PLA/

alginate amalgams and the plain PLA constructs were treated with different concentrations of recombinant human transforming growth factor-betal (TGF-beta 1) either continuously (10 ng/mL) or only for the initial 3 days of culture (50 ng/mL). Chondrogenesis was assessed at weekly intervals with cultures maintained for up to 3 weeks. Histological and immunohistochemical analysis of the TGF-beta 1-treated PLA/ alginate amalgam and PLA constructs showed development of a cartilaginous phenotype from day 7 to day 21 as demonstrated by colocalization of Alcian blue staining with collagen type II and cartilage proteoglycan link protein. Expression of cartilage specific genes , including collagen types II and IX, and aggrecan, was detected in TGF-beta 1-treated cultures by reverse transcription-polymerase chain reaction analysis. The initiation and progression of chondrogenic differentiation within the polymeric macrostructure occurred with both continuous and the initial 3-day TGF-beta 1 treatment regimens, suggesting that key regulatory events of chondrogenesis take place during the early period of cell growth and proliferation. Scanning electron microscopy revealed abundant cells with a rounded morphology in the PLA/ alginate amalgam. These findings suggest that the three-dimensional PLA/alginate amalgam is a potential candidate bioactive scaffold for cartilage tissue engineering applications. Copyright 2001 John Wiley & Sons, Inc. J Biomed Mater Res 57: 394-403, 2001

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(FILE 'HOME' ENTERED AT 13:39:01 'DN 23 JAN 2003) FILE 'MEDLINE, AGRICOLA, CANCERLIT, SCISEARCH, CAPLUS, MEDICONF' ENTERED AT 13:39:09 ON 23 JAN 2003 26 S PORDUS ALGINATE L1L2 15 DUP REM L1 (11 DUPLICATES REMOVED) 15 SORT L2 PY L3=> d an ti so au ab pi 13 12 3-9 ANSWER 12 OF 15 CAPLUS COPYRIGHT 2003 ACS 1.3 2000:488827 CAPLUS ΑN Dil 133:271550 ТŢ Porous carriers for biomedical applications based on alginate hydrogels SO Biomaterials (2000), 21(19), 1921-1927 CODEN: BIMADU; ISSN: 0142-9612 Eiselt, P.; Yeh, J.; Latvala, R. K.; Shea, L. D.; Mooney, D. J. Macroporous scaffolds are typically utilized in tissue engineering AΒ applications to allow for the migration of cells throughout the scaffold and integration of the engineered tissue with the surrounding host tissue. A method to form macroporous beads with an interconnected pore structure from alginate has been developed by incorporating gas pockets within alginate beads, stabilizing the gas bubbles with surfactants, and subsequently removing the gas. Macroporous scaffolds could be formed from alginate with different av. mol. wts. (5-200 kDa) and various surfactants. The gross morphol., amt. of interconnected pores, and total void vol. was investigated both qual. and quant. Importantly, macroporous alginate beads supported cell invasion in vitro and in vivo. L3 ANSWER 3 OF 15 SCISEAFCH COPYRIGHT 2003 ISI (R) 79:368377 SCISEARCH ТΤ USE OF POROUS ALGINATE MATERIAL ALGIPOR IN TREATMENT OF BURNS SO FHIRURGIYA, (1979) Vol. 1979, No. 8, pp. 86-88. ΑU KUZIN M I (Reprint); SCLOGUB V K; YUDENICH V V; RESHETOV I A; YAKOVLEV G B L3ANSWER 4 OF 15 CAPLUS COPYRIGHT 2003 ACS AN 1987:50599 CAPLUS DN106:50599 ТΤ Porous alginate material SŪ U.S.S.R. From: Otkrytiya, Izobret. 1985, (29), 105-6. CODEN: UFXKAF ΤN Vainerman, E. S.; Lozinskii, V. I.; Rogozhin, S. V.; Raskina, L. P.; Shapiro, L. A.; Yakubovich, V. S.; Bronshtein, B. Yu. A porus alginate material with increased d. and high H2O-retaining capacity is prepd. by mixing a 1-4% scln. of Na alginate with a 1-4% soln. of a Ca salt at a 3:1-8:1 molar ratio of alginate monosaccharide unit to Ca salt. The resulting mixt, is frozen in 3-30 min at -6.degree, to -190.degree., allowed to stand for 1-24 h, thawed, and dried under mech. compression. PATENT NO. KIND DATE APPLICATION NO. DATE SU 1171474 A1 19850807 SU 1983-3600824 19830607 ANSWER 5 OF 15 CAPLUS COPYRIGHT 2003 ACS AN 1986:193214 CAPLUS DN 104:193214 TIPorous alginate with a wound-healing effect SO From: Otkrytiya, Izobret. 1985, (29), 106. CODEN: URXXAF ΙN Vainerman, E. S.; Lozinskii, V. I.; Rogozhin, S. V.; Raskina, L. P.; Shapiro, L. A.; Yakubovich, V. S.; Shenker, M. B.; Komissarova, A. L.; Potapov, V. D.; et al. The resistance of the porous surgical material described in USSR Patent 658148 to an aq. medium is improved by keeping the gel obtained from mixing an aq. soln. of Na alginate with a Ca salt in a frozen state from -20 to -40.degree. for 3-24 h prior to freeze-drying. SK-1636

PATENT NO. KIND DATE APPLICATION NO. DATE A2 19850807 SU 1983-3614921 19830607 PΤ SU 1171476 ANSWER 6 OF 15 CAPLUS COPYRIGHT 2003 ACS 1988:57576 CAPLUS AN 108:57576 TТ Porous alginate moldings Jpn. Kokai Tokkyo Koho, 4 pp. CODEN: JEXXAF ΤN Hirasa, Okihiko Porous moldings useful in culturing of enzymes, microbes, etc. are prepd. by heating aq. alginates with aq. poly(vinyl Me ether) (I) to the phase transition temp. (T) of I adding aq. metal salts forming insol. alginates, and extg. I with water at temps. below T. A mixt. of 1 part 5% Na alginate and 1 part 30% I was coated (0.5 mm) on glass, dipped for 10 min in 2% CuSO4 at 40.degree., removed from the glass, and extd. with water to give a Cu alginate film with pore diam. 10-50 .mu. and water permeability 70 times that of a film prepd. without I. PATENT NO. KIND DATE APPLICATION NO. DATE - - -- -----------JP 62250040 A2 JP 05053826 B4 JP 1986-93833 19860423 19871030 19930811 ANSWER 7 OF 15 CAPLUS COPYRIGHT 2003 ACS L3 1993:630640 CAPLUS 119:230640 Low-density polymeric materials having high porosity and surface areas for TΙ metal recovery by extraction SO PCT Int. Appl., 73 pp. CODEN: PIXXD2 ΙN Unger, Peter D.; Fohrbach, Ronald P. AB The porous polymers having an open-cell structure with d. <1.0 g/cm3 and pore vol. .gtoreq.0.5 cm3/q can be prepd. from a gel-forming material or derived from a natural or synthetic polysaccharide, and can be modified for recovery of metal values from fluid streams (esp. by extn.). The synthetic polymers have sp. surface area .gtoreq.85 m2/g (or .gtoreq.200 m2/g if prepd. from chitosan), and are suitable for use in extn. columns. The porous polymers can be manufd. from a gel preform by replacing the gelling solvent with a crosslinking solvent, adding a crosslinking agent, and sepn. of the polymer from the residual solvent. The polymers can be modified for removal of org. or inorg. pollutants, or optionally carbonized for other applications. Thus, porous alginate pellets were manufd. with bulk d. of 0.042 g/cm3, sp. surface area 200 m2/g, pore vol. 2.917 cm3/g, and av. pore size 517 .ANG.. The porous pellets were suitable for extn. of Cd2+, Ni2+, Pb2+, Cu2+, and Cr3+ ions present at 10-1000 ppm in aq. test solns. APPLICATION NO. DATE PATENT NO. KIND DATE ----_ _ _ _ _ _ _ _ _ _ _ _ _ WO 9312877 A1 19930708 PΤ WO 1992-US10567 19921209 W: JP FW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE A1 19941123 EP 1993-900963 19921209 EP 625070 B1 19980708 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE
 JP 06511197
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 19980715
 AT 1993-900963
 19921209
 AT 168040 T3 19980916 ES 1993-900963 ES 2118219 19921209 US 5525710 A 19960611 US 1994-304617 19940912 ANSWER 8 OF 15 MEDLINE AN MEDLINE Porous alginate -- poly (ethylene glycol) entrapment system for the cultivation of mammalian cells. BIOTECHNOLOGY PROGRESS, (1997 Sep-Cct) 13 (5) 569-76. Journal code: 8506292. ISSN: 8756-7938. Seifert D B; Phillips J A AΒ A novel gel entrapment method has been developed where macropores are created within alginate beads to provide an environment for high-density growth of mammalian cells. The method takes advantage of an interaction

between poly(ethylene glycol) (PEG) and alginate to provide a network of pores within the bead for growth while the surrounding alginate matrix retains the integrity of the bead and minimizes cell leakage. Hybridomas were grown to a density approaching 10(8) cells/mL of beads in this system, while conventional alginate restricted growth to a maximum of 2×10^{-5} 10(7) cells/mL of beads. In addition, cell leakage was minimal even at high cell densities, which was not the case with the conventional alginate system. Study of the conventional system determined that cell growth was limited by the alginate matrix; increasing the alginate concentrations resulted in lower final cell densities. In contrast, the PEG-alginate system permits growth in pores so the alginate matrix serves only as a structural matrix for cells. The pore size can be varied as a function of PEG concentration (10-20 wt % PEG) to provide radially defined areas for cell growth and radial diffusion pathways for nutrients/products in the adjacent alginate matrix. Because the PEG-alginate entrapment process does not require additional chemical reactions or temperature changes, the system offers a simple alternative to attain high cell densities in an immobilized bead system. As an illustration of the concept, cells entrapped in this system were grown to high density in both batch and perfusion modes for the production of monoclonal antibodies. Using the suspension batch culture as the base case, the specific monoclonal antibody production rate increased 1.6-fold for the slower growing batch-immobilized culture and 3-fold for the immobilized perfusion culture.

- L3 ANSWER 9 OF 15 SCISEARCH COPYRIGHT 2003 ISI (R)
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- TI Controlled release of interleukin-2 for tumour immunotherapy using alginate/chitosan porous microspheres
- SO JOURNAL OF CONTROLLED RELEASE, (3 JAN 1997) Vol. 43, No. 1, pp. 65-74. Publisher: ELSEVIER SCIENCE BV, PG BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.

ISSN: 0168-3659. ΔII Liu L S; Liu S Q; Ng S Y; Froix M; Ohno T; Heller J (Reprint) AΒ Porous microspheres were formed by the gelation of two polysaccharides, a polyanionic sodium alginate and a polycationic chitosan, followed by lyophilization which creates the porous structure. Porous microspheres were also formed by gelation of sodium alginate with CaCl2 and gelation of sodium alginate with polylysine. FITC-BSA was incorporated into the microspheres by mixing the protein with the polysaccharide solution prior to gelation. Interleukin-2 (IL-2) was incorporated into the preformed microspheres by diffusion from an external aqueous solution of IL-2. Sustained release of the proteins from porous alginate /chitosan microspheres is of longer duration than from alginate/CaCl2, or from alginate/polylysine microspheres. Activity of the released IL-2 was investigated by determining the induction of cytotoxic T lymphocytes (CTL) when incubated with tumor cells and lymphocytes. It was found that the IL-2 remained active in the alginate/chitosan microspheres since the released IL-2 triggered induction of CTL. Further, IL-2 released in a sustained manner triggered induction of CTL more efficiently than free IL-2. Tumor-killing specific activity of CTL was the same whether induced by the sustained released IL-2 or by the addition of free IL-2.